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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,818	04/12/2001	Pnina Fishman	2786-0170P	1935

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EXAMINER

LEWIS, PATRICK T

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 04/20/2004

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/832,818

Applicant(s)

FISHMAN, PNINA

Examiner

Patrick T. Lewis

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16, 36 and 37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16, 36 and 37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 14.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in Paper No. 8 dated November 8, 2002 is acknowledged.
2. Applicant's election of species without traverse in Paper No. 10 dated December 23, 2002 is acknowledged.

Applicant's Response dated June 30, 2003

3. In the Response filed June 30, 2003, claims 1-2, 4, 9-10, and 12 were amended; claims 17-35 were canceled; and claims 36-37 were added.
4. Claims 1-16 and 36-37 are pending. An action on the merits of claims 1-16 and 36-37 is contained herein below.
5. The objection to the specification set forth in the Office Action dated January 28, 2003, has been withdrawn.
6. The rejection of claims 1-16 and 27-35 under 35 U.S.C. 112, first paragraph, has been withdrawn.
7. The rejection of claims 9-16 under 35 U.S.C. 112, first paragraph, has been withdrawn.
8. The rejection of claims 1-16 and 28 under 35 U.S.C. 112, second paragraph, has been withdrawn.
9. The rejection of claim 1 under 35 U.S.C. 102(b) has been withdrawn.

10. The rejection on claims 27-35 under 35 U.S.C. 102(b) has been rendered moot.
11. The rejection of claims 1-16 under 35 U.S.C. § 103(a) is maintained for the reasons of record set forth in the Office Action dated January 28, 2003.

Objections/Rejections of Record Set Forth in Office Action

Dated January 28, 2003

12. Claims 1-16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al. *Experimental Cell Research*, **1997**, Vol. 233, pages 187-197 (Williams) and Jacobson et al. US 5,773,423 (Jacobson).

Applicant's arguments filed June 30, 2003 have been fully considered but they are not persuasive. Applicant argues that one of ordinary skill in the art would have no reason to combine Williams with Jacobson since Jacobson teaches modification of adenosine to moderate A3 selectivity, while Williams teaches away from adenosine receptor binding.

The examiner respectfully disagrees. Applicant's attention is directed to Jacobson column 1, line 43 to column 2, line 8, wherein the motivation is provided to create A3-selective compounds. Jacobson teaches that it is believed that A3-selective compounds will have utility in the therapeutic and/or prophylactic treatment of cardiac disease, infertility, kidney disease, and CNS disorders. Jacobson further teaches that the modification of adenosine at the 5'-position and/or at the N⁶-position with groups that enhance A3 potency has been found to result in moderate A3 selectivity. In the absence of some proof of a secondary nature to obviate the rejection as set forth in the

Office Action dated January 28, 2003, or of some specific limitations which would tip the scale of patentability in the favor of the instantly claimed invention, it would have been obvious to one of ordinary skill in this art at the time of the invention to modify the 2-chloroadenosine of Williams to enhance the activation of natural killer cells.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al. *Experimental Cell Research*, **1997**, Vol. 233, pages 187-197 (Williams) and Jacobson et al. US 5,773,423 (Jacobson) in combination.

Applicant claims methods to activate natural killer cells and methods for therapeutic treatment through activation of natural killer cells via an adenosine A3 receptor agonist. In particular, applicant claims a method for treatment wherein the

disease is associated with malignant cells or cells infected with viruses, bacteria or protozoa.

Williams teaches that 2-chloroadenosine, an adenosine receptor agonist, activates natural killer cells, as exhibited by increased BLT activity. See Abstract.

Williams does not specifically disclose that the N⁶-(2-iodobenzyl)-5'-N-methyluronamide derivative of 2-chloroadenosine, nor any other adenosine A₃ receptor agonist, would activate natural killer cells.

Jacobson teaches that modification of the adenosine at the 5'-position and/or at the N⁶-position will moderate A₃ selectivity. See column 2, lines 64-66. In particular, in column 2, line 67 thru column 3, line 7, Jacobson discloses that the 5'-methyluronamide (IB-MECA) is 50-fold more selective for A₃ versus either A₁ or A₂ receptors.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the 2-chloroadenosine of Williams to enhance the activation of natural killer cells. A skilled artisan would have been motivated and had a reasonable expectation of success to derivative 2-chloroadenosine with 5'-methyluronamide and the N-benzyl group, either alone or in combination, to increase the affinity in binding to A₃ receptors, as per Jacobson.

16. Claims 1-16 and 36-37 are pending. Claims 1-16 and 36-37 are rejected. No claims are allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

Art Unit: 1623

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

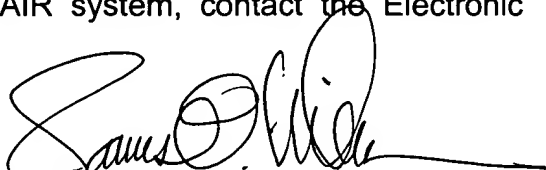
Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623



James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

ptl
April 18, 2004